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– CASES REPORTS –

Challenges in the management of DLBCL in Pregnancy – A Case Report

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Abstract

Introduction: Lymphomas comprise a heterogeneous group of lymphoid malignancies and represent the fourth most common malignancy diagnosed during pregnancy.

Methods: This study explores the diagnostic and therapeutic challenges of diffuse large B-cell lymphoma in the gestational context.

We present the case of a 29-year-old female patient, without comorbidities, diagnosed with non-Hodgkin diffuse large B-cell lymphoma at 24 weeks of gestation. During the antepartum period, she was administered CHOP chemotherapy without rituximab, considering the potential lymphodepleting effects of rituximab and the increased risk of fetal infection. Postpartum treatment included one cycle of R-Hyper-CVAD and four cycles of R-CHOP, resulting in a complete metabolic response on PET-CT (Deauville score 1).

The pregnancy resulted in the delivery of a live preterm infant at 34 weeks via Cesarean section. At the 6-year follow-up, the child exhibits age-appropriate growth and development. The patient remains in complete remission five years post-diagnosis.

Conclusions: The diagnosis and treatment of malignant non-Hodgkin lymphoma during pregnancy represent a challenge, requiring an extensive multidisciplinary approach. Treatment decisions depend heavily on the patient's medical history and the gestational trimester and need a high standard of therapeutic management.

Keywords: Diffuse large B-cell lymphoma; pregnancy; treatment

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most frequent subtype of non-Hodgkin lymphoma (NHL), accounting for approximately one-third of all NHL cases globally [1]. It arises from the neoplastic activation of mature B cells within the germinal centers of the lymph nodes. The disease may manifest with nodal involvement (liver, kidneys, bone marrow, and the central nervous system) or extranodal involvement (most commonly gastrointestinal). The majority of patients (60–70%)

present in an advanced stage characterized by rapid disease progression [2].

The diagnosis of DLBCL may be delayed due to the clinical overlap with certain physiological manifestations specific to pregnancy, such as anemia, leukocytosis, and exertional dyspnea. The treatment, compared to solid neoplasms, is based on potentially teratogenic systemic chemotherapy, instead of surgery or local interventions [3]. The treatment decision takes into consideration a series of aspects related to the stage of the disease, the

aggressiveness of the disease, the trimester of pregnancy, and the patient's option [4].

Case presentation

We present the case of a 29-year-old female patient, with no known comorbidities, who initially presented to a territorial hospital at 16 weeks of gestation, where routine laboratory tests revealed elevated liver enzymes. An abdominal ultrasound was performed, identifying a tumor mass in the left upper quadrant (LUQ).

The diagnostic workup was completed with abdominal and pelvic MRI, which evidenced a retroperitoneal tumor mass (T1/T2 isointense, multiloculated with a pseudonodular appearance, invading the fascial planes, involving the pancreas, great vessels, and the common iliac artery, and tracking along the psoas muscle) and splenomegaly.

To confirm the diagnosis, a biopsy of a left supraclavicular lymph node was performed. The histopathological examination revealed the effacement of the nodal architecture by diffuse proliferation; medium-to-large sized cells exhibiting polymorphism, with rounded nuclei and prominent nucleoli; frequent mitotic and apoptotic figures; isolated binucleated tumor cells and tingible body macrophages. Immunohistochemistry tests confirmed a mature B-cell tumor proliferation (diffuse expression of CD20, CD79a, PAX5), suggesting a diagnosis of diffuse large B-cell

lymphoma, with a very high Ki-67 proliferative index (95%). To determine the cell of origin (COO), the Hans algorithm was applied: CD10 was positive, indicating a germinal center B-cell (GCB) origin. The tumor immunoprofile excluded the activated B-cell (ABC) COO subtype (negative for BCL-2, MUM1/IRF4) and other potentially similar neoplasms (negative for CD30, CD3, AE1/AE3, TdT). The diagnosis of DLBCL, GCB-like subtype, was confirmed.

The patient was admitted to the Hematology Department of the Fundeni Clinical Institute Bucharest. Clinical examination revealed a good general status, ECOG performance status of 0, mild sclero-tegmentary pallor, an ongoing second-trimester pregnancy (24 weeks), and a palpable tumor mass in the LUQ.

Laboratory findings showed a hemoglobin level of 9.3 g/dL, hematocrit of 23%, MCV of 85 fL, a platelet count of 414,000/ μ L, and a white blood cell count of 7,890/ μ L. The differential count was as follows: 2% myelocytes, 12% band neutrophils, 70% segmented neutrophils, 1% basophils, 5% lymphocytes, and 5% monocytes.

Biochemical analysis showed normal hepatic and renal function, with an elevated lactate dehydrogenase of 449 U/L and an elevated alkaline phosphatase of 241 U/L. Viral screening was negative for HBV, HCV, HIV, and HTLV. The temporal evolution of laboratory parameters is shown in Figure 1.

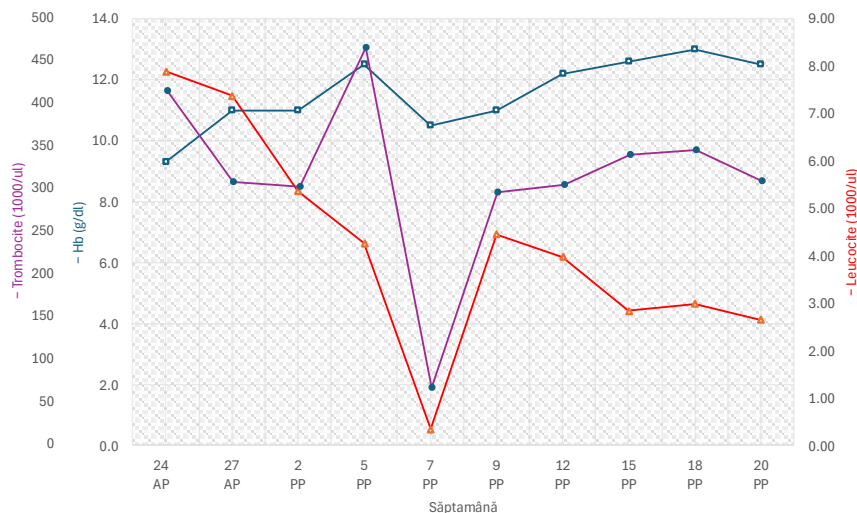


Figure 1. Trends in laboratory parameters over time

A diagnosis of Stage IVA DLBCL, according to the Ann Arbor classification, was established. The patient received a standard chemotherapy protocol consisting of three

cycles of CHOP during the antepartum period. An imaging reassessment was performed after two cycles, with an MRI conducted at 27 weeks of gestation (interpreted in comparison with the previous

MRI from week 16) to provide an evaluation on the treatment response Figure 2.

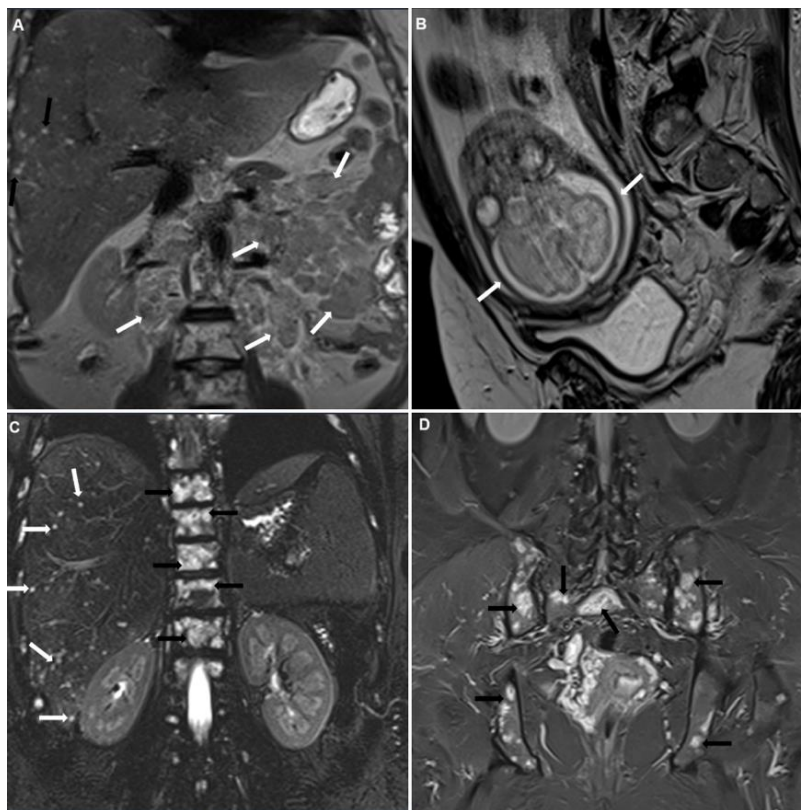


Figure 2 Antepartum MRI examination

A) Coronal T2-weighted sequence – multiple lymphadenopathies with a tendency toward confluence, forming mesenteric adenopathic masses in the left hemiabdomen and the para-aortic region (white arrows); several small hyperintense hepatic nodular lesions on T2 (black arrows);

B) Sagittal T2-weighted sequence centered on the pelvis – ongoing pregnancy, visualizing the cranial extremity of the fetus (white arrows);

C) Coronal STIR sequence of the abdomen – multiple pseudonodular and patchy bone lesions, some confluent, showing marked STIR hyperintensity, located in the lumbar spine (black arrows); hepatomegaly with multiple millimetric nodular lesions showing STIR hyperintensity within the hepatic parenchyma (white arrows), likely in the context of the primary disease;

D) Coronal STIR sequence centered on the pelvis – multiple pseudonodular lesions with marked STIR hyperintensity located in the pelvic bones, suggestive of secondary bone malignancies (black arrows) associated with the primary disease.

The MRI report noted a significant regression of the lymphadenopathy: lombo-aortic nodes decreased from 34 mm to 16 mm, and the intramesenteric ones decreased from 74 mm to 54 mm. However, the liver dimensions increased from 20.5 cm to 24.4 cm, with the emergence of multiple new subcentimetric lesions.

Regarding the skeletal lesions, a significant numerical and dimensional progression was

observed, involving the vertebrae, ribs, sacrum, coxal bones, and femur.

The complete postpartum CT scan (chest, abdomen, and pelvis) provided a comprehensive overview of the current disease status and the response to the antepartum treatment Figure 3.

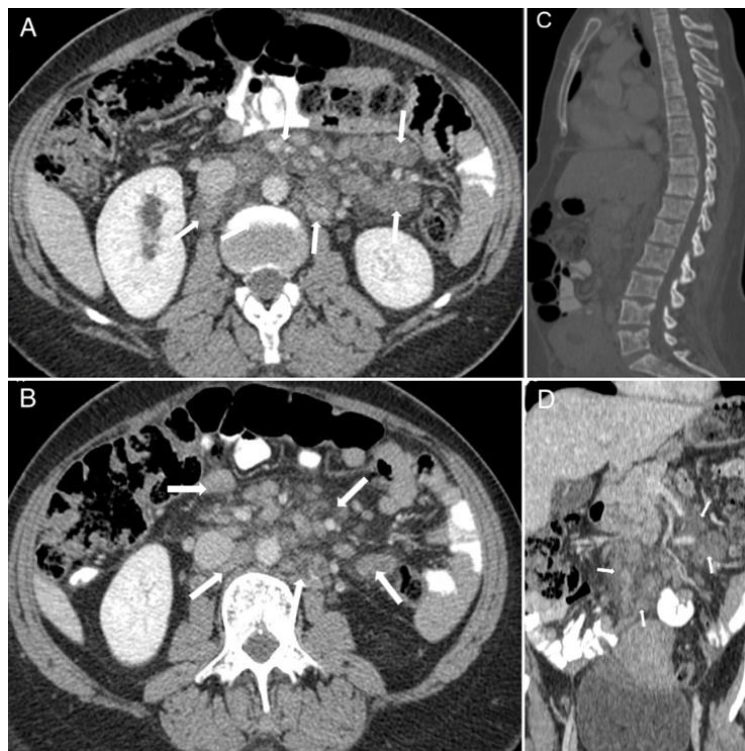


Figure. 3 Postpartum CT examination

A,B) Post-contrast examination, venous phase – abdominal lymphadenopathies located in the mesenteric and para-aortic regions, showing slight regression compared to the prenatal MRI examination (white arrows);

C) Sagittal reconstruction, bone window – inhomogeneous appearance with diffuse osteosclerosis/osteocondensation of the vertebral bodies, featuring multiple pseudonodular osteosclerotic areas (all hyperdense/whiter areas are affected zones) and confluent patches, likely post-therapeutic;

D) Coronal reconstruction, post-contrast venous phase – residual, confluent lymph node masses located within the mesentery and lumbar-aortic region

The radiologist compared the CT findings with the previous MRI examination and observed a generalized progression of the lymphoproliferative process: active disease in both nodal and extranodal sites, persistence of significant lymphadenopathy (conglomerates exceeding 3 cm), significant hepatomegaly with a compressive effect on the portal vein, and diffuse skeletal involvement.

Rituximab was not administered at the initiation of treatment, considering its lymphodepleting effect and the lack of sufficient data in the medical literature regarding the administration of Rituximab during pregnancy.

Based on the CT results, it was decided to initiate one cycle of R-Hyper-CVAD, a more intensive and aggressive chemotherapy protocol than CHOP, and which includes rituximab, to induce remission. Following this R-Hyper-CVAD cycle, a PET-CT was performed.

The PET-CT interpretation showed a favorable response to the oncologic treatment: the lymph node involvement and bone lesions were metabolically inactive, with no radiotracer uptake in the lungs or mammary glands.

A complete metabolic remission was achieved, with a Deauville score of 1.

Following the PET-CT results, therapy was continued with 4 cycles of R-CHOP. The complete remission was obtained and delivery was scheduled at 34 weeks of gestation, without any obstetric or neonatal complications.

Discussion

The decision to employ chemotherapy during pregnancy is individualized. Depending on the gestational trimester and the stage of the disease, various treatment options exist for the management of DLBCL. Standard chemotherapy regimens, such as CHOP or R-CHOP, have been successfully administered during the second and third trimesters to the majority of patients, with minimal maternal complications and no fetal impairment, although with an increased risk of preterm birth and low birth weight [5].

Regarding the first trimester of pregnancy, multi-agent chemotherapy regimens are contraindicated, as treatment is associated with a high risk of congenital malformations [3]. The initiation of chemotherapy should be postponed until the second trimester to allow for the completion of organogenesis [5].

The inclusion of Rituximab in treatment protocol DLBCL in pregnancy improves overall survival (OS) with a rate of 73.3% compared with 60.6% in patients with advanced -stage disease [6]. However, rituximab must be used with caution during pregnancy due to the potential risk of fetal infection and hematologic abnormalities; placental transfer, mediated by immunoglobulin receptors, increases concurrently with gestational age [6].

Chakravarty et al. [7] identified 14 cases of pregnancy with neonatal hematologic or infectious complications. Among these, ten neonates presented with hematologic manifestations, three with infectious manifestations, and one with both. Hematologic complications included B-cell depletion, leukopenia, lymphopenia, neutropenia, thrombocytopenia, anemia, and the detection of rituximab in the umbilical cord blood. Described infectious complications included vertically transmitted CMV hepatitis, bronchiolitis, acute chorioamnionitis, and fever of viral etiology. Table 1 presents four selected cases of NHL from [7] treated with rituximab.

Table 1. Pregnancies complicated by hematological or infectious abnormalities following rituximab therapy during pregnancy

Case	Age	Medical History	Rituximab Dose	Pregnancy Outcome	Hematologic Abnormality / Infection	Follow-up
1	37	Conception within 1 month of rituximab administration	375 mg/m ² weekly x 4 cycles	Female, 40 weeks	Low granulocyte count / None	Normalized in 18 months; normal response to vaccinations
2	35	R-CHOP administered at 16 weeks of gestation	375 mg/m ² weekly x 4 cycles	Female, 41 weeks	Rituximab in cord blood, B-cell depletion / None	Resolved by 12 weeks
3	31	R-CHOP administered at 15 weeks of gestation	375 mg/m ² every 2 weeks x 6 cycles	Female, 33 weeks	Low B-cells at birth, normal immunoglobulins / None	Resolved by 12 weeks
4	33	Patient treated with R-CHOP prior to pregnancy	375 mg/m ² every 2 weeks	Male, 35 weeks	None / Bronchiolitis	Not reported

Data regarding lymphoma in pregnancy are limited and primarily derive from case reports, retrospective studies, or patient registries. The rarity of pregnancy-associated lymphoma precludes the execution of large-scale management and prognostic studies.

The most significant published series include the cohort described by Maggen et al. [6], featuring 80 patients diagnosed with NHL during pregnancy; the series of 90 lymphomas diagnosed during pregnancy described by Evens et al. [8]; and a smaller study by Aviles et al. involving 16 cases [9]. Ciaccio et al. [10] also reported a cohort of 73 patients, of whom 41 were diagnosed antenatally and 32 postnatally, while the series by On et al. [11] describes the effects of rituximab treatment in 37 patients diagnosed with lymphoma during pregnancy.

These studies included data from registries spanning extended periods, some covering several decades, and originated almost exclusively from Western regions, primarily Europe, North America, Australia, and New Zealand

In our study, we obtained a dataset by querying the PubMed database for the period 2019–2026, using the following combination of keywords: ("Lymphoma, Large B-Cell, Diffuse"[MeSH] OR "DLBCL") AND ("Pregnancy"[MeSH] OR "Pregnancy Complications, Neoplastic"[MeSH] OR "pregnant"), identifying 17 articles. For the analysis, data such as patient characteristics, symptoms, and treatment strategies were extracted and entered into

Table 2. Reported cases in the literature (2019–2026) regarding diffuse large B-cell lymphoma (DLBCL) and related entities (such as PM-BCL), diagnosed during pregnancy or in the immediate postpartum period

Authors (Year)	Age/GA	Symptoms/Reason for Presentation	Localization	Diagnosis	Therapeutic Strategies	Observations
Hattori et al. (2019) [12]	31 / 11w	Dyspnea. Massive mediastinal tumor with tracheal compression.	Mediastinum	PM-LBCL	Corticosteroid pulse therapy + VCP (vincristine, cyclophosphamide, prednisolone) with dyspnea relief. Subsequently, 8 cycles of R-CHOP starting from GW 13.	Delivery at 35w 6d without major complications; healthy newborn. Mother in complete remission.
Şükür et al. (2019) [13]	28 / NA	Admitted for fertility preservation prior to oncological therapy (R-CHOP) for DLBCL.	NA	DLBCL. Pregnancy diagnosed incidentally on day 6 of ovarian stimulation (RS-COH).	Ovarian stimulation.	Pregnancy diagnosed incidentally. Termination of pregnancy was decided after the completion of the ovarian stimulation protocol.
Codacci-Pisanelli et al. (2019) [14]	37 / NA	DLBCL diagnosis at 4 months postpartum. Patient ceased breastfeeding for chemotherapy excretion study.	NA	DLBCL	6 cycles of R-CHOP every 21 days, plus Allopurinol during treatment.	Due to the persistence of doxorubicin, doxorubicinol, and cyclophosphamide in breast milk, breastfeeding is contraindicated for at least 6 weeks after the last dose.
Hashimoto et al. (2019) [15]	28 / 15w	Superior Vena Cava Syndrome. Gigantic mediastinal mass (Thoracic CT: 11.0 × 5.2 × 8.7 cm) with compression of the trachea and aortic arch.	Mediastinum	PM-LBCL	3 cycles of CHOP (from GW 16); 3 cycles of R-CHOP (from GW 25). Treatment interrupted at GW 31. Postpartum: 2 cycles of DA-EPOCH-R.	Delivery at 36w 1d. Apgar 7/8. Mother in complete metabolic remission.
Hersey et al. (2020) [16]	38 / 27w	Onset of dysphagia and dysphonia (1 week). Rapidly progressing cervical mass.	Left thyroid lobe (US: 4.4 cm nodule).	DLBCL	Chemotherapy deferred until postpartum. 4 cycles of R-CHOP every 21 days starting on postpartum day 2 with lactation protocol (10+10).	Vaginal delivery at 34w 4d. Apgar 8/9. Patient completed 4 cycles of R-CHOP with maintained remission. Mother and son doing well.
Goto et al. (2020) [17]	32 / 31w	Age 31: Left breast mass and regional lymphadenopathy. Age 32: Pregnancy and relapse (left breast). 2 months postpartum: newborn with disseminated subcutaneous masses.	Mother: Left breast and axillary LN. Newborn: Generalized subcutaneous masses, lymphadenopathy, and multiple hepatic lesions (PET-CT).	DLBCL	Mother (Age 31): R-Hyper-CVAD and R-CHOP. Relapse: Chemotherapy and allogeneic HSCT. Newborn: Intensive chemotherapy and cord blood transplant at 6 months.	Cesarean section at 35w. Apgar 4/7. Identical lymphoma histology (materno-fetal transmission) confirmed by HLA haplotype studies. Mother in complete remission.

Anusim et al. (2020) [18]	28 / 1st Trim.	Dysuria and pelvic pain (6 weeks onset). 7 cm tumor in the anterior vaginal wall involving the urethra.	Vagina (limited disease).	DLBCL	6 cycles of R-CHOP starting at GW 12.	Cesarean section at 37w. Apgar 8/9. Local residual disease; referred for radiotherapy consultation.
Dunleavy et al. (2020) [19]	37 / 30w	Chest pain and dyspnea; right calf cramps. Superior Vena Cava Syndrome.	Mediastinal mass (11.5 × 8.3 × 8.3 cm). Obstruction of SVC and left pulmonary artery.	PM-BCL	High-dose steroids for SVC syndrome. 1 cycle antepartum + 5 cycles postpartum of DA-EPOCH-R therapy.	Vaginal delivery at 35w without complications. PET/CT confirmed complete metabolic remission.
Hernández Martínez et al. (2021) [20]	28 / 15w	Cervical pain and left laterocervical mass. Bulky mediastinal mass invading supraclavicular and axillary spaces.	Mediastinum and Brachial Plexus.	Unclassifiable B-cell lymphoma (intermediate features between DLBCL and HL).	1st line: 6 cycles CHOP (partial response). 2nd line: Brentuximab-ESHAP (no response). 3rd line: R-ICE.	Elective Cesarean section at 30w. Apgar 8/9. Mother was on 3rd line chemotherapy at the time of publication.
Horner et al. (2022) [21]	34 / 14w	Chronic pain in the left ankle and calcaneus. 1.5 cm circumferential soft tissue mass at the calcaneus.	Left calcaneus.	DLBCL	20 sessions of localized radiotherapy to the left calcaneus during the 3rd trimester.	Full-term delivery. Patient remains in remission 9 years post-diagnosis.
Gowda et al. (2023) [22]	24 / 9th Month	Painful left breast mass simulating an abscess (1-month history).	Postpartum: 9.6 cm retroareolar mass; systemic lymphadenopathy and extranodal involvement (liver, thyroid).	PB-DLBCL	Refused treatment during pregnancy. Postpartum: Emergency wound debridement, excisional biopsy, and 2 cycles of R-CHOP.	Death occurred after 2 cycles of chemotherapy.
Lahlimi et al. (2025) [23]	20 / NA	3 months postpartum/lactating. Bilateral breast nodules, rapid enlargement, and painful tension.	Bilateral breasts. Progression to liver, kidney, bone, peritoneum, and CNS.	PB-DLBCL	1st line: 4 cycles R-CHOP (no response). 2nd line: 2 cycles R-ICE.	Rapid progression of gigantomastia under treatment. CNS dissemination. Death 4 months after diagnosis.
Hori et al. (2026) [24]	39 / 31w	Persistent chronic frontal sinusitis; suspected Pott's puffy tumor. Palpable edema of the central forehead.	Frontal sinus with intracranial extension; metastatic disease in cervical, thoracic, and lumbar spine.	LBCL with IRF4 rearrangement	Postpartum: 6 cycles of MR-CHOP, Cyberknife radiotherapy, and intrathecal Cytarabine.	Labor induction and delivery prior to chemotherapy. No evidence of disease at 2-year follow-up.
Yoshida et al. (2026) [25]	34 / 16w	Dyspnea and cardio-respiratory arrest. Massive mediastinal tumor.	Mediastinum	Mediastinal DLBCL	1st line: Empiric R-CHOP (no response). 2nd line: 2 cycles of DA-EPOCH-R.	Patient opted to continue pregnancy; second fatal cardio-respiratory arrest occurred at GW 24.

Table 2. Due to a lack of diagnostic specifications, details regarding maternal treatment, or information about the fetus, three cases were excluded

Two cases from the table data are of particular interest: one concerning the excretion of cytostatics into breast milk and the other regarding the transplacental transmission of tumor cells from mother to fetus.

In the first case, Codacci-Pisanelli et al. [14] analyzed the excretion of cytostatic drugs into breast milk in a 37-year-old patient diagnosed four months postpartum with aggressive lymphoma (Stage IV DLBCL), who was undergoing the standard R-CHOP chemotherapy protocol.

A total of 290 breast milk samples were collected during chemotherapy. Measurements revealed measurable concentrations of cyclophosphamide, doxorubicin, doxorubicinol, and other metabolites in the analyzed samples for at least 21 days following administration. Doxorubicinol reached concentrations ten times higher than doxorubicin. Vincristine was not detected in any of the tested samples, and rituximab was not measured.

Due to the prolonged persistence of cytostatics and their metabolites in breast milk, the authors conclude that breastfeeding should be completely avoided during treatment and for at least six weeks after the final dose.

In the second case, Goto et al. [17] analyzed an extremely rare clinical occurrence involving the transplacental transmission of tumor cells from mother to fetus in a 31-year-old patient diagnosed with DLBCL. She received R-Hyper-CVAD as initial chemotherapy, followed by R-CHOP, achieving complete remission. The patient delivered via Cesarean section at 35 weeks of gestation and began postpartum chemotherapy, resulting in complete remission.

Two months postpartum, the neonate presented with generalized subcutaneous masses, and a diagnosis of DLBCL was confirmed. The identity between the maternal and neonatal tumors was established through short tandem repeat (STR) analysis of specific genetic markers and by studying HLA haplotypes.

In the case we presented, six years after delivery, the child exhibits normal development and progression for their age, without secondary complications from prenatal chemotherapy exposure and without associated congenital pathologies. The patient remains in complete remission five years after completing chemotherapy.

Conclusions

In the case presented, the therapeutic strategy proved successful: treatment commenced with CHOP to ensure pregnancy safety. Taking into consideration the progression of the disease, the therapy was followed by an escalation to R-Hyper-CVAD postpartum and continued treatment with 5 cycles of R-CHOP and obtained complete remission.

The diagnosis and treatment of malignant non-Hodgkin lymphoma during pregnancy remain a significant challenge, requiring an extensive multidisciplinary approach. The primary objectives are to bring the pregnancy to term without teratogenic or neoplastic complications, achieve complete remission for the mother, and ensure the delivery of a live infant. Treatment decisions depend heavily on the patient's medical history, the gestational trimester, and a high standard of therapeutic management.

Ethics Statement and Conflict of Interest Disclosures

Financial support and sponsorship: All authors have declared that no financial support was received from any organization for the submitted work.

Ethics Consideration:

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national laws. Written informed consent was provided by the participant in this study.

Conflict of interest:

No known conflict of interest correlated with this publication.

Availability of data and materials:

The data used and/or analyzed throughout this study are available from the corresponding authors upon reasonable request.

Competing interests:

The authors declared that they have no competing interests.

The use of generative AI and AI-assisted technologies: AI technologies were used solely to refine English language and spelling.

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